Remarks

Claims 1, 2, 4, 5, 8, 11, 13-15 and 20-30 are pending in the application for which a Request for Continued Examination (RCE) is filed herewith. This amendment is a submission under 37 C.F.R. 1.114(c) that responds to issues presented in the Office action dated February 5, 2007. Claims 1, 2, 4, 5, 8 and 20-30 stand rejected and claims 11 and 13-15 are withdrawn from consideration. A Notice of Appeal and petition for extension of time were filed with authorization to debit all required fees from Assignee's account on July 5, 2007.

In this amendment, claims 1, 4, 5, 8, 13, 14, and 15 have been amended to delete "about" referring to percentage base differences. No new matter has been added by these amendments. Applicants respectfully request entry of the amendments to the claims and reconsideration of the application in view of the amendments and the remarks that follow.

Claim Rejections under 35 U.S.C. § 102

To be anticipated by prior art, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Res. Fndn. v. Genentec, Inc.*, 927 F.2d 1565, 18 U.S.P.Q.2d 1001, 1010, 18 U.S.P.Q.2d 1896 (Fed. Cir. 1991).

Claims 1, 2, 5, 8 and 22 stand rejected under 35 U.S.C. 102(e) based on the disclosure of Gudibande et al. (U.S. Patent 5,597,910), based on Gudibande et al.'s SEQ ID NO:4 which is structurally related to Applicants' SEQ ID NO:5, on Gudibande et al.'s SEQ ID NO:6 which is structurally related to Applicants' SEQ ID NO:45, and on Gudibande et al.'s SEQ ID NO:5 which is structurally related to Applicants' SEQ ID NO:121. Gudibande et al. was also cited for teaching hybridization of an oligonucleotide to a target in a PCR reaction (with regard to dependent claim 2) and for teaching labeled (biotinylated) probes (with regard to dependent claim 22).

With regard to claim 1 (and its dependent claims), which recites SEQ ID NO:5, Gudibande et al. was cited for teaching SEQ ID NO:4, an oligonucleotide (3PV16) specific for HPV16 DNA (col. 20, ll. 16 and 19-23), which shares a subsequence region of 21 nt of 100% identity with a subsequence of Applicants' SEQ ID NO:5. The Examiner stated that the prior art sequence has an actual difference of 25% compared to the claimed sequence, but stated that the phrase "about" referring to a 10% base difference was broadly interpreted to encompass the larger difference.

Claim 1 has been amended to delete "about" in the phrase "about a 10% base difference" which overcomes the rejection of claim 1 and dependent claims 2, 5, 8 and 22 with regard to compositions that include SEQ ID NO:5. Applicants, therefore, seek allowance of amended claim 1 and its dependent claims 2, 5, 8 and 22.

With regard to claim 5, Gudibande et al. was cited for teaching an HPV 18 specific oligonucleotide (3PV18) of SEQ ID NO:6, which is an oligonucleotide for amplification of HPV18 DNA (col. 20, ll. 14-34), that shares a subsequence region of 22 nt of 100% identity with a subsequence of Applicants' SEQ ID NO:45. The Examiner stated that the prior art sequence has an actual difference of 29% compared to the claimed sequence, but stated that "about" referring to a 10% base difference was broadly interpreted to encompass the larger difference.

Claim 5 has been amended to delete "about" in the phrase "about a 10% base difference" which overcomes this rejection. Applicants, therefore, seek allowance of amended claim 5.

With regard to claim 8, Gudibande et al. was cited for teaching SEQ ID NO:5, which was disclosed as a biotinylated oligonucleotide specific for capture of amplified HPV18 products (col. 20, ll. 14-34). The reverse complement of Gudibande et al.'s SEQ ID NO:5 shares a subsequence region of 23 nt of 100% identity with a subsequence of Applicants' SEQ ID NO:121. The Examiner stated that the prior art sequence has an actual difference of 28% compared to the claimed sequence, but

stated that "about" referring to a 10% base difference was broadly interpreted to encompass this difference.

Claim 8 has been amended to delete "about" in the phrase "about a 10% base difference" which overcomes this rejection. Applicants, therefore, request allowance of amended claim 8.

Claims 1 and 2 stand rejected under 35 U.S.C. 102(e) based on the disclosure of Bouma et al. (U.S. Patent 5,484,699). The rejection of claim 1 is based on Bouma et al.'s SEQ ID NO:95 (col. 22, Example 19) which is structurally related to Applicants' SEQ ID NO:5, and the rejection of claim 2 on the teaching formation of a hybrid with a target region during an amplification reaction (col. 22, Example 19).

Bouma et al.'s SEQ ID NO:95 is structurally related to Applicants' SEQ ID NO:5, in that Bouma et al.'s SEQ ID NO:95 shares a subsequence region of 20 nt of 100% identity with a subsequence of Applicants' SEQ ID NO:5. The Examiner acknowledged that the prior art sequence has an actual difference of 26% compared to the claimed sequence, but stated that "about" referring to a 10% base difference was broadly interpreted to encompass the larger difference. Bouma et al.'s teaching of primer hybridization to a target sequence was cited in rejecting claim 2, which depends from claim 1.

Claim 1 has been amended to delete "about" in the phrase "about a 10% base difference" which overcomes the rejections of claim 1 and dependent claim 2. Applicants therefore request allowance of amended claim 1 and claim 2.

Claim Rejections under 35 U.S.C. § 103

Determination of whether an invention would have been obvious under § 103 is a legal conclusion based on underlying factual findings. *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000). The framework for applying § 103 includes a determination of the: (1) scope and content of the prior art; (2) differences between the prior art and the

claimed invention; and (3) level of ordinary skill in the pertinent art. *Graham v. John Deere Co. of Kansas City.*, 383 U.S. 1, 17-18 (1966), aff'd in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ___ (April 30, 2007). If all the elements of an invention are found in a combination of prior art references, a proper analysis under § 103 further requires consideration of whether the prior art would also have revealed that those of ordinary skill would have a reasonable expectation of success in making the claimed composition or carrying out the claimed process. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991) (citing *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988)); *In re O'Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988).

Once an invention is made, the prior art can often, in hindsight, be seen to provide some support for its success. But "selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings." *In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). That is, it is impermissible to use hindsight that relies on an applicant's disclosure to pick and choose features of a claimed invention from the prior art to create the claimed invention. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

Objective indicia of non-obviousness include the prior art teaching away from the claimed invention. *United States v. Adams*, 383 U.S. 39 (1966). A reference must be considered as a whole and must be considered for all that it teaches. *W.L. Gore & Associates v. Garlock*, 721 F.2d 1540 at 1550 (Fed. Cir. 1983). Teaching in the prior art that discourages persons of skill in the art from an approach leading to the claimed invention must be considered because doing what those skilled in the art said should not be done is strongly probative of nonobviousness.

Claims 1, 2, 4, 5, 8 and 20-30 stand rejected under 35 U.S.C. 103(a) based on the disclosures of Brown (WO 94/26934) in view of Gudibande et al. (U.S. Patent 5,597,910) and further in view of Hogan et al. (U.S. Patent 5,030,557) and further in view of Dopazo et al. (*J. Virol. Meth.*, 1993, vol. 41, pp. 157-166).

Brown was cited for teaching a composition for amplifying an HPV16 target nucleic acid (p. 11, ll. 25-27), specifically SEQ ID NO:27 (HPV120 oligonucleotide), formation of kits (p. 4, ll. 23-24), and sequences that comprise Applicants' SEQ ID nos. 1, 5, 45, 85 and 121 (SEQ ID NO:1, shown on pp. 24-26, citing specific starting points with regard to SEQ ID Nos. 1, 5 and 85; and SEQ ID NO:2, on pp. 26-28, citing specific starting points with regard to SEQ Nos. 45 and 121).

Gudibande et al. was cited with regard to claims 20, 21, 23, 24, 26, 27, 29 and 30 for teaching sequences that will hybridize to HPV 16, citing the structural relationship of Gudibande et al.' SEQ ID NO:4 and Applicants' SEQ ID NO:5 (as described under §102 rejections) and, with regard to claim 2, for teaching hybrid formation. Gudibande et al. was cited with regard to claims 5, 26, 27, 29 and 30 for teaching SEQ ID NO:6 which is structurally related to Applicants SEQ ID NO:45 (as described under §102 rejections). With regard to claims 8 and 29, Gudibande et al. was cited for teaching SEQ ID NO:5 which is structurally related to Applicants' SEQ ID NO:121 (as described under §102 rejections). With regard to claim 22, Gudibande et al. was cited for teaching labeled probes (e.g., biotinylated).

Hogan was cited for teaching methods for enhancing hybridization by using helper probes of certain characteristics (col. 4, ll. 44-68 and col. 5-6).

Dopazo et al. was cited for teaching an available computer program to select any primers which are common to a group of sequences but to exclude primers which are non-specific (spanning pp. 159-160), and a suggestion to select HPV primers (p. 157).

In making the rejections under § 103, the Office action described a process by which a person having ordinary skill in the art at the time of the invention might have combined selected portions of the cited teachings. The Office action concluded that Applicants' claimed oligonucleotides are considered structural homologs derived from sequences suggested in the prior art which a biochemist of ordinary skill would attempt to obtain as alternate compounds with improved properties (pp. 10-12).

Brown teaches a nucleic acid hybridization probe assay for detecting mRNA encoded by HPV16 or HPV18 that includes subjecting a sample to nucleic acid amplification by using a first and second primer, transcribing the DNA made by use of the primers, hybridizing the amplified mRNA to a capture probe to form a capture complex that is attached to a solid phase, then hybridizing a type-specific enzyme-conjugated detection probe to the amplified RNA, and reacting the conjugated enzyme with a substrate to produce a detectable signal (p. 3, l. 13-p. 5, l. 20). Brown also teaches oligonucleotides used in development of the assays (p. 10, l. 6-p.12, line 6). Brown teaches sets of primers, of which at least one must contain a promoter sequence (p. 12, l. 13-17). Brown teaches "primer families" made up of a promoter primer and two or more other primers, from which a preferred primer set is made (p. 12, l. 25-p.14, l. 2). Primer families are described by combinations of numbers (see p. 13, l. 5-9) which refer to oligonucleotides listed as "Primer Probes" on pages 10-12 (which includes SEQ ID Nos.), where they are described by the number preceded by "HPV" (e.g., primer "120" is referred to as "HPV120" in the list and identified as SEQ ID NO:27 on page 11, line 25). For example, in the description (p. 13, ll, 5-6) "The primer family for 120 is 29 and 90" means a primer group made up of promoter primer HPV120 (SEQ ID NO:27) with primers HPV29 (SEQ ID NO:6) and HPV90 (SEQ ID NO:16) (see p. 10, ll. 18 and 33). Other oligonucleotide sequences used in the assay are described as capture probes ("CAP"), detection probes ("DET") and Positive Hybridization Control Probes ("PHC") (see pp. 15-16).

Brown teaches a composition for amplifying HPV16 (spanning pp. 12-13) that uses an amplification oligonucleotide that includes a 5' promoter sequence, specifically SEQ ID NO:27 (HPV120), but Brown's target specific sequence of the promoter primer is unlike Applicants' disclosed sequences. Brown teaches at least eight primer families to amplify HPV 16 sequences (p. 13, ll. 5-9 and 14-20), in which each family includes a promoter primer. Describing primer families or pairs that include a promoter primer,

however, does not disclose Applicants' specific sequences that may include a promoter attached to the target specific sequence. As stated by the Examiner (p. 6, ll. 15-17), Brown does not teach Applicants' SEQ Nos. 1, 5, 45, 85, and 121, or the use of helper probes.

The Examiner pointed to specific subportions of Brown's SEQ ID NO:1 (570 nt HPV 16 genomic sequence encoding E6/E7 polypeptides) that includes Applicants' SEQ ID Nos. 1, 5, and 85 (reverse complement). The Examiner pointed to specific subportions of Brown's SEQ ID NO:2 (483 nt HPV18 genomic sequence encoding E6/E7 polypeptides) that includes Applicants' SEQ ID Nos. 45 and 121. Brown, however, does not direct a person of ordinary skill to the subportions of these larger genomic sequences that comprise Applicants' sequences. Unless one were provided with Applicants' disclosure, one would not have arrived at Applicants' sequences based on the teachings of Brown because Brown's own method did not direct Brown to arrive at Applicants' sequences contained in the larger genomic sequences.

Merely adding a 5' promoter sequence to an HPV specific sequence selected by using Brown's method would not lead a person of ordinary skill in the art to make Applicants' claimed invention. A person of ordinary skill in the art provided with Brown's disclosure would use Brown's HPV target region and method to select primer families and sets (p. 12, l. 9-13) to arrive at the same combinations Brown disclosed. That is, the skilled person would use the primer families/sets taught by Brown because Brown has already performed Brown's selection method to identify preferred oligonucleotides for amplification and detection of HPV 16 and HPV18 sequences in the disclosed genomic sequences.

Gudibande et al. was cited for teaching sequences that direct the ordinary practitioner to probes that overlap Applicants' claimed oligonucleotides (related to claims 5, 8, 20-21, 23-24, 26-27, 29, and 30, based on sequence comparisons as in rejections under §102), for teaching hybrid formation (related to claim 2), and for

teaching labeled probes (related to claim 22).

Gudibande et al. teach a method of detecting a nucleic acid analyte by using specific labeled compounds (referred to as "Tag-phosphoramidite"or "phosphoramidite label" or "tag-NHS ester"), which are incorporated in amplification reactions (col. 2, ll. 49-58, and col. 9, l. 46-col.10, l. 51). Gudibande et al.'s examples describe oligonucleotides, labeling methods, characterization of labeled oligonucleotides, and use of labeled oligonucleotides in amplification reactions. Gudibande et al. describe oligonucleotides specific for HPV16 (col. 20, ll. 14-25) along with other oligonucleotides specific for HPV18, Lambda, and HIV sequences, and nonspecific sequences (PV6). Examples IX to XIII (col. 24-27) describe experiments in which HPV16 specific oligonucleotides were used in single primer amplification reactions in which the time course, optimal temperature, and sensitivity of reactions were characterized. The HPV 16 primer was 3PV16 (SEQ ID NO:4) labeled with tag-NHS ester (col. 24, ll. 39-40).

Although some of Gudibande et al.'s oligonucleotide sequences overlap with Applicants' sequences, Gudibande et al.'s disclosure must be considered for all it teaches. Gudibande et al. primarily teach methods and compounds for labeling oligonucleotides. Gudibande et al.'s HPV16 specific oligonucleotides are used as a single labeled primer in amplification reactions (3PV16) or as a biotinylated probe (2PV16, col. 24, ll. 45-50) for capture of the amplified products. Gudibande et al. teaches specialized reactions in which a labeled primer is used (e.g., col. 25, ll. 38-42 and col. 27, ll. 64-67), and in which "each particular template-primer combination has a different temperature optimum" (col. 26, ll. 25-29), indicating that changes in a primer can affect its functionality. Biotinylated probe is used to capture the amplified product for detection. A person of ordinary skill in the art of molecular biology would not be motivated to make Applicants' compositions or methods by the disclosure of Gudibande et al.'s two exemplary HPV16 sequences that are used in specialized one-primer amplification methods that rely on a labeled primer (SEQ ID NO:4) and a labeled

capture probe (SEQ ID NO:3). That is, mere structural similarity between sequences would not have motivated the skilled person to select an oligonucleotide of a related sequence that does not include critical structural features taught by Gudibande et al. (tag-NHS ester or phosphoramidite labels or biotinylation), to create the claimed inventions.

Applicants also note that the Examiner's statements in the Office action (under §102 rejections) about the "actual difference" between the specified claimed sequences and an overlapping prior art sequence appear to calculate a minimum difference between the compared sequences. The Office action calculation appears to only account for additional bases in Applicants' sequence compared to the reference sequence, then divided by the total bases in Applicants' sequence. A more complete calculation takes into account all of the differences between the claimed and reference sequences (i.e., additions or omissions of bases at both ends relative to Applicants' sequence). For example, a complete calculation of differences should add 3' bases included in Applicants' sequence that are not in the reference sequence plus 5' bases included in the reference sequence that are not in Applicants' sequence, divided by the total bases in the claimed sequence. For example, Applicants' SEQ ID NO:5 compared with Gudibande's SEQ ID NO:4 was stated in the Office action to have an "actual difference" of 25% which represents the 3' bases in Applicant's sequence that do not appear in the reference sequence (7 nt) divided by the total bases (28 nt) of the claimed sequence ($7 \div 28 = 0.25$). In contrast, a complete calculation of differences totals the 3' bases of the claimed sequence that do not appear in the reference sequence (7) plus the 5' bases of the reference sequence that do not appear in the claimed sequence (9), divided by the total bases (28) of the claimed sequence, i.e., $[7 + 9] \div 28 = 0.57$ or 57% actual difference. Similar calculations performed for other claimed sequences compared to those of Gudibande et al. cited in the Office action are:

(1) for Gudibande et al.'s SEQ ID NO:6 compared to claimed SEQ ID NO:45, the

total 5' + 3' bases differences between the two sequences divided by the total bases in the claimed sequence is [8 + 9] ÷ 31 = 0.54, or 54% actual difference, and

(2) for the reverse complement of Gudibande et al.'s SEQ ID NO:5 compared to claimed SEQ ID NO:121, the total 5' + 3' bases differences between the two sequences divided by the total bases in the claimed sequence is [7 + 9] ÷ 32 = 0.50 or 50% actual difference. Applicants respectfully submit that these calculations more accurately describe the differences between the prior art sequences and those claimed. Based on Gudibande et al.'s statement that each particular template-primer combination demonstrated an optimal amplification temperature (col. 26, ll. 25-29), the person having ordinary skill in the art would not have been motivated to seek out other overlapping sequence because of the unpredictability of characteristics associated with each hybridized complex. That is, the person of ordinary skill would have relied on Gudibande et al.'s optimization of compositions and methods for HPV16 (and HPV18) amplification and detection, which were distinguishable as taught in the reference.

Hogan et al. was cited for teaching use of helper probes to enhance hybridization and requirements for helper probes. A helper oligonucleotide binds to a targeted nucleic acid, usually without substantially overlapping the region bound by a probe, to enhance hybridization kinetics between the probe and the sequence in the targeted nucleic acid to which it is complementary and/or to raise the Tm of the hybrid between probe and its complementary sequence (col. 5, l. 64-col.6, l. 4). A skilled person provided with Hogan et al.'s teachings would only select an appropriate helper oligonucleotide *after* the probe sequence has been selected because the helper oligonucleotide functions relative to its associated probe. That is, a person of ordinary skill in the art would have to know which probes Applicants had selected to be motivated to select a helper probe for use with the selected probes because the helper probe is determined relative to its probe. To have a reasonable expectation of arriving at Applicants' invention, the skilled person would have to know Applicants' probe

selections which influence the selection of helper oligonucleotides. Other helper probes besides SEQ ID NO:121 might be chosen based on Hogan et al.'s teachings (col. 5, l. 64-col. 6, l. 4, col. 7, ll. 14-49). Thus, absent Applicants' disclosure of selected probes, the skilled person aware of the teachings of Hogan et al. would have no reasonable expectation of success at creating Applicants' claimed compositions or methods.

Dopazo et al. was cited to provide evidence that the ordinary practitioner in 1993 would have had access to a computer program that can select primers which are common to a group of sequences but to exclude non-specific primers. Although the Office action (p. 9, ¶ 3) stated that "Dopazo specifically suggests selection of primers in HPV (see page 157)", that section of the reference merely states that PCR has been used in diagnosis of viral infections and "Specific detection of DNA viruses has been achieved, among others, for human papilloma viruses ...." That is, Dopazo et al. do not suggest use of their computerized algorithm for selection of HPV-specific primers.

The Office action (p. 9, ¶ 3), relying on the disclosures of Brown and Dopazo et al., concluded that:

> "An ordinary practitioner, motivated by Brown to select primers to detect HPV 16 or 18, would have been able to utilize the available computer program of Dopazo to select primers that were species specific, of which SEQ ID Nos. 1, 5, 45, 85 and 121 are simply structural equivalents . . .."

Applicants respectfully disagree with that conclusion based on other teachings in the cited art about the unpredictability of oligonucleotides (Gudibande et al., discussed above), the relatively large actual differences between claimed and disclosed sequences (discussed above), and based additional arguments that follow.

Dopazo et al. teach a particular computer program ("PCRDiag") that followed certain primer selection rules (see pp. 159-160) and applied them in three different modes (see p. 159, last paragraph). The algorithm sequentially examines sequences for their compliance with primer selection rules and ultimately constructs a list of pairs of

selected primers (pp. 160-161). In one example, the output obtained from computerized examination of a 500 base target region (FIG. 1) showed that the algorithm selected nine different primer groups and 26 pairs of primers. But Dopazo et al. provide no indication that *any* of the primer pairs *functioned* in specific amplification of the intended target. Examination of the "search conditions" shown at the top of FIG. 1, moreover, shows that half of Applicants' primers would not have been selected by Dopazo et al.'s algorithm because of their size and GC content (SEQ ID Nos. 1-4 are 28 nt each and 28.5% GC content). Further examination of FIG. 1shows that the GC content of primers within a group was relatively similar. For example, in the eighth group that includes the most members (Antisense 502 and six Sense primers) and the widest Tm range (56-70°C), the GC content of all the primers in the group was relatively similar (52-65%, mean = 56 ± 4.4). Dopazo et al.'s algorithm likely would not have selected primer pairs like Applicants that paired sequences with a relatively low GC content (SEQ ID Nos. 1-4) with sequences with a relatively high GC content (SEQ ID Nos. 85-88, 52% GC). Thus, Applicants' arrived at the claimed compositions by using an approach that Dopazo et al.'s disclosure would have discouraged persons of ordinary skill in the art from taking, which is strongly probative of nonobviousness of Applicants' selections.

In making the obviousness rejections, the Examiner combined teachings from Brown (a target region and method for selection of primer sequences), Gudibande et al. (locations of primers based on shared sequences), Hogan et al. (probe detection that includes use of helper probes), and Dopazo et al. (computerized algorithm to select primer pairs). After selecting certain features from these references and combining them in a way to suggest Applicants' inventions, the Office action concluded that Applicants compositions are simply "structural homologs which are derived from sequences suggested in the prior art" and that "a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties." This process of

picking and choosing elements from the prior art and combining them in a certain way to arrive at the claimed inventions, however, appears to rely impermissibly on the use of hindsight based on Applicants' disclosure. The claimed inventions are different than the compositions and methods taught in the prior art. The prior art already disclosed compositions, which although different from Applicants, functioned for detection of HPV 16 and HPV 18 (e.g., Brown and Gudibande et al.) so the skilled biochemist would simply have followed the teachings of the prior art and used the disclosed and optimized compositions and methods. If the skilled biochemist were motivated to obtain alternate compounds, there is no reason for that skilled person to have deviated from the teachings of Brown (i.e., use of Brown's method to select the HPV16 specific oligonucleotides disclosed by Brown), or from the teachings of Gudibande et al. (selection and use of single primers labeled with tag-NHS ester or phosphoramidite in a single-primer amplification system followed by capture of amplified product by using biotin labeled probes), or from the teachings of Dopazo et al. (use of a computerized algorithm to select primer groups in a narrow %GC range). If the skilled person were motivated to modify or combine the cited art teachings, that person could have done so in many other ways. For example, based on Brown's teaching of a 570 nt HPV 16 genomic sequence and Dopazo et al.'s algorith, the person would expect to generate 9 to 10 groups of primers for this target region comprised of about 26 or more primer pairs (based on Dopazo et al.'s FIG. 1 which located 9 groups and 26 pairs in a 500 nt target), all of which in a group would be approximately the same size and %GC. Then, the skilled person could choose a single primer from primers selected by either the method of Brown or Dopazo et al. and use them as taught by Gudibande et al.. That is, each selected primer would be labeled with a tag-NHS ester and incorporated in a single primer amplification, followed by and capture of the amplified products by using a biotinylated probe. None of the disclosures of Brown, Gudibande et al., or Dopazo et al. suggest that the skilled person would include a helper oligonucleotide as taught by

Hogan et al., so that feature appears to have been selected by use of hindsight based on Applicants' disclosure.

Even if all the elements of a claimed invention are found in a combination of prior art references, which is not the case here because of the differences described above, a proper analysis requires consideration of whether the prior art would also have revealed that those of ordinary skill would have a reasonable expectation of success in making the claimed composition or carrying out the claimed method. With so many possible features, potential sequences, and method steps that might have been selected and combined in a variety of ways by a person of ordinary skill in the art based on the cited art, it is unlikely that the person of ordinary skill would have had a reasonable expectation of arriving at Applicants' invention unless that skilled person were provided with Applicants' disclosure.

Applicants, therefore, respectfully submit that a *prima facie* case of obviousness has not been made and request withdrawal of the rejections of claims 1, 2, 4, 5, 8 and 20-30 under § 103. Applicants seek allowance of the claims as amended herein.

Related Applications

This application is related to a co-pending application of U.S. Serial No.10/607,416, filed June 26, 2003 by the same inventors, which was previously disclosed, for which a RCE was filed September 5, 2007.

Assignee of this application is also the assignee of another co-pending application that has claims drawn to compositions and methods for detection of nucleic acid sequences of multiple human papillomavirus (HPV) types, which is U.S. Serial No. 11/296,931, filed December 8, 2005.

Fee Authorization

Authorization is hereby provided to debit any and all fees due in connection with this submission and the accompanying RCE from Deposit Account No. 07-0835, maintained in the name of Gen-Probe Incorporated.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully submit that the claims, as amended, are patentable and in condition for allowance. Accordingly, withdrawal of the rejections and allowance of the application is earnestly solicited. The undersigned has made a good-faith effort to address all the points raised in the last Office action and to place the claims in condition for continued examination and allowance. If minor matters remain that could be resolved by a telephone interview, the Examiner is invited to contact Applicants' representative at the number below.

Respectfully submitted,

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By: Christine A. Gritzmacher
Christine A. Gritzmacher
Registration No. 40,627
Attorney for Applicants

GEN-PROBE INCORPORATED
Patent Department - Mail Stop #1
10210 Genetic Center Drive
San Diego, California 92121
Tel.: 858-410-8927 FAX: 858-410-8928